Personalized medicine and fair allocation of resources: Do we set the right priorities?

EACME Annual Conference
„Personalised Medicine“ – medicine for the person? Ethical challenges for medical research and practice
Bochum, 19-21 September 2013
Personalized medicine – a “new“ paradigm?!

PM: field with (analytically) no clear boundary ⇒ object of inquiry??

Systematic literature search ⇒ 2457 articles with PM/IM in title/abstract ⇒ 683 articles with one or more definitions!

- analysis of components + quality criteria of definitions
- cf. Sebastian Schleidgens paper at 16:30 (sess. 5)

Definition:

*PM seeks to improve stratification of health care by utilizing biological information and biomarkers on the level of molecular disease pathways, genetics, proteomics as well as metabolomics*

De facto: patient subgroups ⇒ *stratified medicine*
Three methodological elements

(1) Literature review
(2) Analytic investigation
(3) Qualitative interview study with experts & stakeholders in the German healthcare system

Schleidgen and Marckmann *BMC Medical Ethics* 2013, 14:20
http://www.biomedcentral.com/1472-6939/14/20

Open Access

Re-focusing the ethical discourse on personalized medicine: a qualitative interview study with stakeholders in the German healthcare system

Sebastian Schleidgen* and Georg Marckmann
## Ethical Implications of PM: Overview

### Areas of personalized medicine

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<td>Higher risks due to insufficient testing</td>
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<td>Informed consent for add-on-studies</td>
<td>Implication of predictive information for individual</td>
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<td>Overemphasis of individual responsibility for health</td>
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<td>Allocation of research resources</td>
<td>Discrimination of „bad risks“</td>
<td>Cost impact? =&gt; Access, distributive justice</td>
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<td>Study design (patient relevant outcomes)</td>
<td>(Access, distributive justice)</td>
<td>(Discrimination of bad responders)</td>
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**ORIGINALARBEIT**

*Alter Wein in neuen Schläuchen? Ethische Implikationen der Individualisierten Medizin*

Sebastian Schleidgen · Georg Marckmann

DOI 10.1007/s00481-013-0267-3

Georg Marckmann, LMU  
19.09.13  
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## Distributive justice: 4 levels

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Level 1: Allocation of resources into PM (vs. other alternatives)

- Central issue: high public and private investment in PM \( \Rightarrow \) right priorities?
  - Directed towards priority health needs of the population?
  - Higher health gain if resources are invested in other approaches?
  - Does it take into account existing inequalities in health status?

Policy options:

1. Explicit priority setting in public funding for research
   - Health care needs in an ageing society (chronic diseases, multi-morbidity)
   - Priority for disadvantaged (sub-)populations
   - Potential for improving health status in population
   - Priority for common diseases?
   - Cost-effectiveness (efficiency) – anticipative assessment possible?

2. Incentives for pharmaceutical companies to invest in areas with high priority
Level 2: Resource allocation *within* PM

- Investment in profitable areas ⇒ populations with rare (genetic) profile are neglected ⇒ „orphan populations“
- Neglect of vulnerable, already disadvantaged subpopulations
- Research with patient subgroups beyond PM neglected ⇒ higher risks through insufficiently tested interventions

Policy options

- Incentives for investments by pharmaceutical industry in „orphan populations“ (cf. current orphan drug regulation)
- More public research funding in (genetically) rare patient populations
- Challenge: increasing number of „orphan drugs“ ⇒ increasing public spending necessary ⇒ limits? priorities?
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Justice 

requires: General & equal access to personalized medicine

Central question: *Will health care become more or less expensive with PM?*

**Optimistic scenario:** *Cost savings* through targeted therapies with a higher effectiveness and less side effects

**Pessimistic scenario:** *cost increase* due to additional (biomarker) diagnostic, high costs for R&D and production of PM for small populations (“niche busters”)

*Cost increase* $\Rightarrow$ (potentially) limited access for less affluent patients with less comprehensive insurance coverage

$\Rightarrow$ Creation of new & aggravation of existing inequalities (on a national and global scale!)
Cost-effectiveness depends on several factors:

- Size of target population
- Number & cost of biomarker tests (i.e. test strategy)
- Likelihood of modified treatment decision due to diagnostic
- Cost impact of modified treatment decision

▷ Cost-effectiveness varies considerably! (Wong et al. 2010)
▷ Individual assessment of C/E-ration for each PM intervention
▷ **Shape the cost-effectiveness of PM!**

▷ HNPCC-screening: between 20,000€ and 1,500,000€/LYS depending on test strategy! (Mayer & Rogowski 2011)

**Challenge (e.g. in oncology):**

- Small incremental benefit ⇒ bad cost-effectiveness (HER-2 & Trastuzumab: $125,000/QALY [Elkin et al. 2004])

▷ Does the (small) additional benefit (at the end of life) justify the high costs?
Cost-benefit-assessment requires valid benefit assessment!

At the time of licensing of the drug: benefit under routine conditions difficult to assess

- Studies for licensing: usually assess efficacy under ideal conditions
- Selected, not representative samples
- Surrogate endpoints instead of patient relevant endpoints (overall survival, quality of life)
- No head-to-head comparison with standard treatment
- Incomplete data transparency (reporting & publication bias)

_requirements for a needs oriented and fair allocation & distribution are often not met!
Policy options

(1) First: Improve benefit assessment
   - Independent, publicly financed clinical studies after licensing of the drug (patient relevant outcomes)
   - (Initially) coverage only in clinical studies („coverage with evidence development“)
   - (Germany: benefit assessment according to AMNOG too early!)

(2) Then: Cost-benefit assessment (CEA/CUA)
   - Price negotiations with pharmaceutical industry
   - Limited of coverage of interventions with bad incremental C/E-ratio
   - Goal: unlimited access to real innovations for all patients, exclusion of „pseudo innovations“

Problem in Germany (& other countries): so far no open socio-political discourse on setting limits fairly in the hc system!
Finally...

I would like to thank

• *you* for your attention
• *my colleagues* in the BMBF-collaborative research project for their input
  • Sebastian Schleidgen (ethics)
  • Elisabeth Meyer/Wolf Rogowski (economics)
  • Simone von Hardenberg/Nikola Wilman (law)

Further Information: [www.igv-ethik.de](http://www.igv-ethik.de)
Slides: [www.dermedizinethiker.de](http://www.dermedizinethiker.de)
Contact: [marckmann@lmu.de](mailto:marckmann@lmu.de)
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Indirect consequences (level 4)

Discrimination of patient subgroups through *secondary* information of PM about

- risk of disease, prognosis, treatment effectiveness
- Categorization: „good responder“ ⇔ „non-responder“, „difficult to treat“

**Fairness implications:**
- Restricted access to health care interventions
- Restricted access to health insurances or higher premiums
- Disadvantages in other areas (e.g. employment)
- Stigmatization of subpopulations

**Policy options**
- Restrictive regulation of access to sensitive (genetic) information (e.g. only physician & patient, patient controls access)
- Informed consent for testing: Information about (indirect) risks
Conclusion

Personalized medicine has (potentially) ethical implications
★ most are not specific for PM
★ depend on application of individualized strategies

**Individualized prediction & prevention**: mainly challenges on the individual level (excess diagnostic information!)

**Individualized treatment**: mainly challenges on societal level
- Allocation of research resources into/within PM
- Distribution of PM interventions (cost-effectiveness!)

No general rejection of PM, but
1. „Monitoring“ of ethical implications
2. Implement policies to ensure ethically acceptable development and application of PM

Shape the development in the field of PM!